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REVIEW

A Comprehensive Review of Non-Surgical Treatments for Hypertrophic and Keloid Scars in Skin of Color

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Abstract: Hypertrophic and keloid scars are fibroproliferative growths resulting from aberrant wound healing. Individuals with Fitzpatrick skin types (FSTs) IV–VI are particularly predisposed to hypertrophic and keloid scarring, yet specific guidelines for these populations are still lacking within the literature. Therefore, this comprehensive review provides a list of various treatments and considerations for hypertrophic and keloid scarring in patients with skin of color. We constructed a comprehensive PubMed search term and performed quadruple-blinded screening on all resulting studies to achieve this objective. Our findings demonstrate 1) the lack of efficacious treatments for raised scars within this population and 2) the need to empirically investigate individualized and multimodal therapeutic options for those with skin of color.

Keywords: corticosteroid, bleomycin, 5-FU, laser, FST IV-VI, skin of color

Introduction

Hypertrophic scars (HTS) and keloids are two distinct types of scarring that clinically present as raised, firm, and reddened nodules or plaques at a site of previous skin trauma, often associated with pruritus or discomfort.[1,2] Their unique clinical and histopathological features can be explained by a variety of dysregulated extracellular matrix (ECM)-related and inflammatory processes that synergistically drive excess fibrosis.[2] At the cellular level, exaggerated proliferation of fibroblasts and their derivatives—notably myofibroblasts—participate directly in the excess deposition of dermal collagen during HTS and keloid formation.[3] Fibroblast and myofibroblast activities are driven by other key players in the keloid microenvironment, too, including type-1 and type-2 T-helper cells, M2 macrophages, dendritic cells, and natural killer cells.[3] Infiltration of these leukocytes contributes to a microenvironment enriched in inflammatory cytokines, notably transforming growth factor beta (TGF-β), interleukins, etc., which reciprocally upregulate the expression of pro-fibrotic genes.[4]

They have also been understood to result from dysregulated inflammatory processes at the molecular level, which necessarily involves an anomalous response to the wound-healing process.[2] More specifically, it has been hypothesized that errors in the regulation of the inflammatory phase—the first of four stages in the wound-healing process—lead to the formation of these raised scars.[5–7] Excess levels of the pro-inflammatory cytokines IL-6 and IL-8 and insufficient levels of anti-inflammatory cytokine IL-10 have been implicated in skewing this wound-healing process towards excessive collagen deposition and fibrosis.[2] TGF-β also serves a key role in scar formation pathways.[2] This factor is a potent fibrogenic cytokine that directly stimulates fibroblasts to proliferate and increase the synthesis of extracellular matrix components, including collagen.[2] TGF-β1/2 are participatory members in a signaling cascade that leads to fibroblast activation; TGF-β3, unlike its counterparts, is a receptor antagonist in this process.[2] Increased fibroblast activation, due to over-expression of TGF-β1/2 and decreased expression of TGF-β3, leads to ECM collagen deposition, resulting in a hypertrophic or keloid scar response.[2]

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Despite their similar pathologic origins, HTS and keloids are pathologically distinct. Both types of scarring are classically characterized by their raised, indurated, and fibrotic features.[8] Although keloids have the ability to grow beyond the borders of the initial skin injury, hypertrophic scarring is often contained within the site of injury.[9] A histopathological comparative analysis demonstrated that keloid scars have a much more distinct distribution of fibroblasts and lymphocytes along their periphery, a characteristic underlying their persistent growth pattern.[10] Conversely, HTS have a less peripheral but more centralized fibroblast and lymphocytic infiltrate, which may explain their tendency to stagnate or regress.[10] Histologically, a pattern of wavy regularity has been observed in hypertrophic scarring; in contrast, keloid collagen composition is disorganized and demonstrates no repeated pattern.[11]

Perhaps, the most significant shared aspect of hypertrophic and keloid scarring is their disproportionate prevalence in skin of color, operationally defined as Fitzpatrick skin types (FSTs) IV–VI. Compared to other races and ethnicities, individuals of African, Asian, and Hispanic descent are more highly impacted. The incidence of these scarring types within the darker skin population—namely Black and Hispanic populations—is between 4.5% and 16%, compared to roughly 0.09% in FST I.[12,13]

This disproportionate incidence in skin of color is linked to several chromosomal bands, including 10q21.21 and 18q21 in Chinese Han families, 2q23 in a Japanese family, and 7p11 in an African-American family as well as four known single nucleotide polymorphisms (SNPs) across three loci in the Japanese population, including 1q41, 3q22.3–23, and 15q21.3.[14,15] Beyond these potential genetic contributions, however, melanocytes have been implicated in the development of HTS and keloids. Histological studies have suggested that trauma to the skin triggers melanocyte proliferation, which subsequently increases TGF-β production.[16,17] Additionally, melanocytes produce endothelin-1 (ET-1), a peptide that not only regulates melanogenesis but also acts as a mitogen for fibroblasts, further promoting their proliferation and contributing to scar formation.[16] The interaction between melanocytes and fibroblasts may be further mediated by the production of stem cell factor (SCF) by fibroblasts, which binds to the c-Kit receptor on melanocytes, creating a feedback loop that enhances melanocyte survival and function, thereby sustaining this proliferative signal to fibroblasts.[16,17]

In spite of increased incidence in skin of color, the current scientific literature does not seem to focus on FSTs IV–VI. While some studies include these skin types in their research, types IV–VI are underrepresented and often placed in a pool of other participants with unspecified or lighter skin types. In addition, there exist only a few studies which have looked exclusively at skin of color. As a result, it has been challenging to identify the most effective treatments, with consideration given to common adverse effects, for this specific population. In this literature review, we aim to 1) understand the various treatment options for hypertrophic and keloid scarring and 2) discuss plans of management for skin of color.

Corticosteroids

Corticosteroids remain the recommended first-line treatment in the non-surgical management of HTS and keloids.[9] Corticosteroids act to reduce scar volume via multiple mechanisms: 1) decreasing local inflammation, 2) dampening fibroblast proliferation, and 3) inhibiting collagen production.[18,19] On a molecular level, corticosteroids have been found to hinder the expression of TGF-β1, thereby leading to a decrease in collagen synthesis.[20,21]

Triamcinolone acetonide (TAC) is the most frequently employed corticosteroid to treat keloids and HTS.[22] While TAC can also be administered topically or subdermally, the intralesional injection route of administration is preferred for its ability to deliver higher concentrations of medication at the scar site while ensuring minimal systemic absorption.[22] Intralesional administration of TAC is associated with high clinical response rates ranging from 50% to 100% across FSTs.[23,24] However, this efficacy is accompanied by a high likelihood of recurrence, at 33% after one year and 50% after five years.[23] Other corticosteroids that are employed to treat keloids/HTS are betamethasone, TAC ointments, fluocinolone acetate cream, and fludroxycortide tapes.[19]

In addition to high efficacy rates, the widespread acceptance of corticosteroid therapy in clinical practice is attributed to its generally tolerable side effects. The most commonly reported side effects of intralesional corticosteroid injection include mild, transient sequelae like telangiectasias, temporary skin and subcutaneous fat atrophy, pigmentary changes, and ulcerations.[25] Pain associated with the injection, particularly in dense or sensitive keloid scars, is also an acknowledged side effect during treatment.[25] To reduce pain, lidocaine is often mixed with the steroid solution before injection and can be further supplemented by topical numbing agents.[9]

Specific considerations for skin of color also demonstrate why corticosteroids are preferred. First, corticosteroid therapy, across its various administration routes, is considered a minimally invasive approach. Given the increased susceptibility of FSTs IV–VI to HTS and keloids after skin injury, minimizing trauma to the skin is especially relevant when treating patients with darker skin types to potentially lower the risk of recurrence or new scar formation at the treatment site.[26]

While several studies have investigated the efficacy of corticosteroid injection after surgical excision or in tandem with other modalities, few have sought to investigate the monotherapy in FSTs IV–VI. A study by Belie et al, however, showed the success of intralesional TAC over verapamil, a calcium channel blocker, in reducing keloid-associated pain and pruritus in a sample of African patients.[27] While after 6 weeks both groups demonstrated statistically significant reductions in keloid height, TAC more quickly and completely reduced patient-reported symptoms.[27] Although 80% of patients in the TAC group had hypopigmentation and skin atrophy, these side effects were localized to the affected site, whereas patients in the verapamil group suffered from systemic side effects.[27] Khan et al demonstrated a non-statistically significant difference in TAC efficacy for the treatment of keloids across FSTs.[28] They suggest that although corticosteroids might not be as efficacious as antineoplastic drugs like bleomycin, corticosteroids may be a better choice for darker skin types due to fewer pigmentary changes.[28]

Antineoplastic Agents

Several antineoplastic agents have been investigated for their role in treating HTS and keloids. Two commonly used compounds are bleomycin and 5-fluorouracil (5-FU). These drugs are classified as antimitotic because they inhibit cell proliferation and promote apoptosis.[29]

Bleomycin

Derived from *Streptomyces verticillus*, cytostatic drug Bleomycin is used to treat non-integumentary cancer.[30,31] Bleomycin has more recently been repurposed in order to address hyper-fibrotic skin conditions. Bodokh and Brun published a study in 1996 where they noted marked volume reduction and decreased "functional impairment" in several of 31 keloids and 5 HTS following intralesional bleomycin injection.[32] Further studies have confirmed that bleomycin inhibits proteins in the aforementioned TGF-β pathway.

Bleomycin can be administered to the mid-dermal region through several different methods, including intralesional injection, puncture deposits, Dermojet injection, or tattooing.[1] Side effects include transient pain at the injection site and in rarer, more severe cases, ulceration and tissue necrosis.[33–35]

The efficacy of bleomycin for HTS and keloids in skin of color appears relatively well-established in comparison to other treatment methods. One study by Huu et al found that intralesional bleomycin injections were effective in reducing keloid scar volume (70.8% complete flattening) within the Vietnamese population.[36] Even in cases where incomplete flattening was noted, Vancouver Scar Scale (VSS) data demonstrated an 80.8% and 70.3% reduction in pruritus and pain, respectively.[36] Notably, however, pain, hyperpigmentation (56.7%), blistering, and scar recurrence (50% after 18 months) were reported adverse effects.[36] Additional literature has corroborated high rates of hyperpigmentation with bleomycin usage, with one study recording a staggering 76.9%.[37] Combined with a non-statistically significant difference between bleomycin and TAC usage, Moravej et al suggest bleomycin should be used sparingly in darker skin types.[37] Importantly, these studies in particular underscore the prevalence of post-inflammatory hyperpigmentation (PIH) in patients receiving bleomycin injection. Given the increased risk for PIH in skin of color, treatment with bleomycin for this specific patient population warrants both caution and preventative measures.

Despite significant concern of PIH, Payapvipapong et al found that intralesional bleomycin injections reduced the occurrence of skin atrophy for FSTs III–IV relative to intralesional TAC injections.[38] Though their comparative study concluded intralesional bleomycin was no more efficacious than TAC (10 mg/mL) injection in reducing keloid/HTS volume, 0.0% of patients undergoing bleomycin injections experienced the adverse effect of skin atrophy.[38] In using a lower concentration of cytostatic drug (1 mg/mL), ulceration was also avoided.[38]

Further studies which seek to more concretely address both efficacy and undesirable side effects of bleomycin in FSTs IV–VI are warranted.

5-Fluorouracil

The antineoplastic agent 5-fluorouracil (5-FU) is an approved therapy for colorectal and breast cancers; however, off-label use of this drug includes the treatment of HTS and keloids.[39]

On a molecular level, 5-FU is an analog of the pyrimidine uracil. The compound demonstrates remarkable anti-metabolic activity by directly incorporating into the nucleotide sequence during DNA and RNA synthesis.[40] In addition, 5-FU forms an inhibitory ternary complex with thymidylate synthase, a rate-limiting enzyme in the DNA and RNA synthesis process that catalyzes the formation of [deoxy]thymidine monophosphate (dTMP) from deoxyuridine monophosphate (dUMP).[41,42] Such inhibition causes thymineless death, leading to its employment as an effective cancer therapeutic.[43] Due to 1) a lack of these monomeric building blocks via thymidylate synthase inhibition and 2) faulty DNA and RNA as a result of incorporated 5-FU, highly proliferative cells (eg, fibroblasts) are unable to replicate, resulting in scar degradation.[44,45] Thus, keloids and HTS are prime targets for 5-FU treatment.

Many studies have demonstrated the efficacy of 5-FU in the treatment of keloids and HTS; however, few have sought to investigate the monotherapeutic option specifically in FSTs IV–VI. In 2002, Gupta and Kalra demonstrated the successful treatment of keloids in 24 patients (FSTs IV and V) with 50–150 mg intralesional injections of 5-FU, once weekly, for up to 16 weeks or until therapeutic satisfaction.[46] 33.3% of patients demonstrated >75% flattening and about half of participants showed >50% flattening.[46] 70.8% of patients reported decreases in symptoms of pruritus, pain, and discharge, with no recurrence at 3–6 month follow-ups.[46] Importantly, hyperpigmentation was observed in all patients and ulceration in one patient, but all adverse events were found to resolve upon therapeutic cessation.[46]

Further studies are needed in order to establish the efficacy of 5-FU monotherapy and associated side effects in FSTs IV–VI.

Laser Therapy

Laser therapy is a widely used, energy-based treatment modality for skin resurfacing and other integumentary changes. Broadly speaking, lasers can be classified into two distinct categories: ablative or non-ablative. While non-ablative lasers leave the overlying epidermal layer intact, ablative lasers cause epidermal destruction and heating of the dermal layer.[47]

Both categories of laser, however, can be used in the treatment of keloids and HTS. Ablative lasers (eg, CO_2, Er:YAG, and argon types) reduce scar volume by removing layers of scar tissue through interaction of the laser energy with the water in and on the skin.[48] In contrast, non-ablative lasers (eg, Nd:YAG, pulsed-dye laser (PDL), KTP, etc) target hemoglobin in red blood cells, leading to the destruction of microvasculature and ultimately hypoxia in the local tissue environment.[48] This poor oxygenation leads to collagen remodeling and reduction.[49–51] Such phenomena make laser therapy a promising therapeutic agent for keloids and HTS.

Given the prevalence of laser therapy as a staple dermatologic treatment, this energy-based modality has been more robustly studied in skin of color for its keloid and hypertrophic scar-reduction abilities. Evidence-based reviews have suggested that fractional lasers are a safer, more favorable choice when it comes to FSTs IV–VI.[52] Despite this, research with respect to monotherapy in the treatment of HTS and keloids has been minor; there currently exists several more studies which employ laser therapy as one portion of a larger combinatorial treatment.

Adverse Effects

Laser therapy is often cautioned for use in higher FSTs due to the risk of PIH.[53,54] Advances in laser technology have therefore sought to minimize PIH in these susceptible populations. Patients with darker skin are implored to be compliant with both sunscreen and hydroquinone usage prior to and after laser therapy.[55] During treatment, there are also several steps that may be used in order to reduce postoperative complications. These include 1) reducing the number of laser passes and 2) the usage of cooling devices to prevent bulk heating of the treated area(s).[52]

Non-Ablative Lasers

Several different non-ablative laser modalities have demonstrated clinical efficacy with a favorable safety profile in patients of color. In 2013, Rossi et al established the success of a 300 microsecond Nd:YAG laser in the treatment of keloids in a sample (n = 44) consisting of FSTs I–VI.[56] Despite transient post-procedure erythema, Nd:YAG therapy demonstrated superior cosmesis, producing a substantial reduction in scar volume and vasculature in comparison to intralesional

corticosteroid injection.[56] Interestingly, all patients, including those of skin types IV–VI, did not exhibit dyschromia.[56] In a separate study conducted by Koike et al, 102 Japanese patients with steroid-resistant HTS or keloids were all found to have statistically significant changes in post-treatment scores as defined by Japan Scar Workshop (JSW) criteria following Nd:YAG laser therapy.[50] Notably, however, recurrence after six months occurred in 4% of HTS patients as compared to 52.9% of patients with anterior chest keloids, 35.7% of upper arm keloids, and 25% of scapula keloids.[50] The authors suggested that the efficacy of Nd:YAG laser therapy can be diminished for keloids specifically if redness, induration, and mechanical tension are allowed to persist unchecked.[50] Repeated treatment with Nd:YAG laser therapy to overcome these prohibitive factors within this patient population is both warranted and critical for "curative" results.

Several studies have also focused on PDL monotherapeutic interventions. A 2003 study by Kono et al found a 585 nm PDL effective in reducing erythema, texture, and pliability of HTS in Asian patients.[57] Importantly, these researchers alluded to low fluence values and cooling as critical clinical safety practices necessary for implementation when treating skin of color.[57] Additional studies have corroborated a "trend toward better response" for PDL therapy employing lower fluence, early therapeutic intervention, and several treatment sessions, especially for FST VI.[58,59]

It is critical to note, however, that the wavelengths employed by PDL therapy (585 nm and 595 nm) and KTP lasers (532 nm) yield competitive chromophores: oxyhemoglobin and melanin.[60,61] Due to the increased melanin content in higher FSTs, the oxyhemoglobin chromophore may not be targeted with optimal specificity and incidental melanin chromophore absorption of light energy may lead to dyspigmentation.[60,61] The 1064 nm Nd:YAG laser may be a more suitable choice for darker skin types due to reduced competitive absorption.[62]

Ablative Lasers

Lasers of the ablative type–namely CO_2 and erbium-based lasers–have been studied for their efficacy in treating HTS and keloids in FST IV–VI. Fully ablative laser technology for this scarring niche is sparse within the literature, perhaps due to its highly aggressive potential. A more recent alternative–the fractionally ablative laser–has perhaps received more research attention and been given its title as the "gold standard" due to its reduced traumatic impact and quicker healing time.[47]

CO_2 laser therapy has boasted recent success in darker skin types. In 2015, a study by Azzam et al employed a split-scar treatment paradigm using fractional CO_2 laser monotherapy in a group with FSTs II–VI.[63] Using VSS, the researchers established a significant decrease in scar severity on the treated scar portion, mainly attributable to increases in scar pliability, with little changes in pigmentation across all FSTs.[63] Of relevance is the researchers' choice of pulse spacing; for patients with darker skin types, greater intervals were employed, suggesting the importance of tailoring laser parameters on an individual basis in order to combat the greater risks associated with laser therapy in this susceptible patient group.[63] Further studies have elucidated the significance of early therapeutic intervention when treating traumatic scars with fractional CO_2 laser in skin of color in order to improve scar pliability, height, and pigmentation.[64]

The highly aggressive nature of CO_2 laser therapy and its associated side effects served as the impetus for the development of a milder therapeutic: the erbium-based laser.[65] One study employing the 1550 nm Er:Glass laser has shown success in improving pliability, texture, and pigmentation of HTS in FSTs II–IV.[66] The study's patient with skin type IV demonstrated no PIH, supporting the efficacy of the erbium laser in reducing bulk-heating likelihood.[66] Another study investigating Er:YAG for atrophic and hypertrophic scars in FSTs IV and V demonstrated successful height reduction of raised scars, specifically with a short-pulse, ablative functionality.[67] Post-operative side effects consisted of erythema (2.5% of patients) and hyperpigmentation in one patient.[67] All adverse events resolved with photoprotection, sunscreen, lightening cream, and topical steroids.[67]

The comparative efficacy of CO_2 versus Er:YAG laser therapy for the treatment of keloids and HTS in patients of color still remains debated. In a 2023 study, Elsaid et al demonstrated the ability of an Er:YAG laser to reduce vascularity and improve pliability in patients with skin types II–V, whereas CO_2 laser improved pliability and significantly reduced height.[68] Patients treated specifically with Er:YAG revealed replacement of disorganized collagen fibers with parallel organization on histological examination.[68] Notably, in all patients, improvements in pigmentation were noted and no dyschromia was observed.[68]

Consensus among clinicians generally supports the usage of fractional CO_2 laser over erbium-based treatment within the general population; however, this preference reverses specifically for patients with skin of color.[62] For FSTs IV–VI,

the lower risk of PIH favors Er:YAG energy-based devices.[62] Further studies evaluating the comparative efficacy of non-ablative (eg, PDL, KTP, and Nd:YAG), fractionally ablative (eg, CO_2 and Er:YAG), and fully ablative (eg, CO_2 and Er:YAG) monotherapies for keloids and HTS specifically in FSTs IV–VI is warranted.

Combinatorial Treatments

Despite the demonstrated efficacy of energy- and non-energy-based modalities, monotherapeutic application appears to limit maximal results. Therefore, combining diverse therapies with varying operator techniques, treatment intervals, and sequences may enhance patient outcomes.

Minimally Invasive Methods

While these monotherapies appear to be chronically understudied in skin of color, topical applications such as silicone gel sheeting and pressure garments have often been used as adjuvant therapies in addition to more invasive methods (ie, surgery). Silicone gel sheeting is thought to exert its beneficial effects on keloids and HTS by minimizing trans-epidermal water loss.[69] As a result, the stratum corneum remains hydrated, reducing the necessity for the skin to produce inflammatory molecules which would ultimately cause hyperproliferative fibrosis.[69] In contrast, pressure therapy is suggested to modulate hyperproliferative scar properties via mechanoreceptor-induced cell apoptosis as well as compression-based fibroblast ischemia.[70] Li-Tsang et al demonstrated that, 2 months post-intervention, combined silicone gel sheeting and pressure therapies were more effective than the corresponding monotherapies in reducing scar thickness in a Chinese population.[71] At the 6 month mark, however, both the patients receiving the combinatorial treatment and the pressure garment monotherapy showed statistically similar reductions in scar thickness.[71] Further studies are certainly warranted to solidify both the combined efficacy and broader application of these less-invasive modalities in skin of color specifically.

Multimodal Injection Therapy

Injection therapy consisting of various corticosteroids and antineoplastic agents is a common combinatorial treatment. TAC may be mixed with agents such as 5-FU and bleomycin. Reinholz et al found that combinatorial intralesional injection of 5-FU and TAC (3:1) successfully reduced keloid volume, height, and penetration depth.[72] Notable side effects included high rates of hyperpigmentation and telangiectasia.[72] Similarly, in a five-split-scar study, Manuskiatti and Fitzpatrick evaluated the comparative efficacy of 585 nm PDL, TAC, 5-FU, TAC + 5-FU against a negative control.[58] While results in scar volume reduction were similar between monotherapeutics and combinatorials, combinatorial administration of TAC and 5-FU eliminated hypopigmentation, atrophy, and telangiectasia that were associated with sole administration of TAC.[58] Such favorable patient outcomes and minimal associated risk may soon qualify combined injection of TAC and 5-FU as a frontline therapy for skin of color.

Multimodal Laser Therapy

Due to differential mechanisms, the employment of several types of lasers for the treatment of hypertrophic and keloid scars has gained increasing traction over monotherapeutic implementation.

A study exploring the impact of combined CO_2 laser and 595 nm PDL in FSTs III–VI yielded remission in a majority of patients, with 38% showing "good" results and 62% demonstrating "excellent" results.[73] No side effects were observed following treatment; notably, patients pre-treated with a topical lightening agent and pressure therapy was employed following the laser procedure.[73] Another study utilizing the same treatment scheme but with combined Nd:YAG and PDL in a cohort of Chinese patients yielded different results.[74] The authors adjusted laser parameters according to skin type and other patient characteristics, which produced notable improvement with no adverse events reported.[74] Future studies analyzing how laser parameters can affect treatment outcomes are needed to refine current protocols for multimodal laser modalities.

In a separate within-groups study, multimodal approaches proved less optimal compared to monotherapy. Tawfic et al demonstrated significant improvement in VSS and POSAS scores and histological collagen fiber improvement following CO_2, Nd:YAG, or combined CO_2 + Nd:YAG lasers but found statistically non-significant differences between groups.[75] Importantly, scars treated with multimodal therapy revealed a statistically significant increase in hypopigmentation relative to monotherapy, which was attributed to "excessive thermal injury" due to this combination.[75]

Laser Excision with Intralesional Injection

Energy-based devices have also been combined with intralesional injections in order to synergistically treat HTS and keloids. Lasers, when employed as coagulative surgical excision instruments, have also been combined with intralesional injection for enhanced effect.[76] One study demonstrated successful surgical excision of earlobe keloids (POSAS score of 2/10 in 64.28% of patients) in FSTs III–VI with a 980 nm diode laser followed by TAC injection.[77] The researchers selected an injection volume of 0.5–1 mg of TAC in order to avoid both skin atrophy and pigmentary changes.[77] In another study, combined treatment with a 595 nm PDL and intralesional TAC successfully reduced scar height, pigmentation, and vascularity.[60] Treatment with PDL alone yielded similar results, suggesting that TAC was only necessary for reducing the volume of larger hypertrophic scars.[60] Kim et al posit that four to six sessions of treatment are optimal in order to minimize the appearance of superficial blood vessels, which is presumably delayed due to the competitive absorption of thermal energy by off-target chromophores, such as melanin in patients of color.[60]

The type of injection after laser therapy has also been investigated. In one within-groups study, after receiving fractional CO_2 laser treatment, patients with skin of color who were given intralesional TAC showed statistically significant keloid height reduction in comparison to intralesional verapamil.[78] Despite this, the frequency of adverse events such as telangiectasia and skin atrophy was notably higher for those who received TAC.[78]

Laser-Assisted Drug Delivery

An alternative to intralesional injection, laser-assisted drug delivery (LADD) has more recently been employed in the treatment of keloids and HTS. LADD has been praised for its ability to overcome the selective permeability of the skin by allowing for topical absorption of various drugs.[79] The vertical microchannels introduced into the skin–most commonly by fractionally ablative lasers–are thought to facilitate such delivery.[79]

Corticosteroids are frequently used during the employment of LADD. In one study, ablative fractional CO_2 laser was used in the successful topical delivery of 40 mg/mL TAC to HTS of pediatric burn patients (FSTs I–VI).[80] Given the risk for dyschromia, only FSTs I–III received PDL prior to CO_2 laser administration, yet there was no significant difference in POSAS between skin types I–II and IV–VI.[80] All patients demonstrated statistically significant improvements in POSAS-rated scar thickness, pigmentation, pliability, relief, and surface area with no adverse changes in skin pigmentation.[80] No significant improvement in vascularity was reported, which may have been due to the infrequency of vascularity and challenge of identifying erythema in the patient population (67% FSTs IV–VI).[80]

In another study of HTS in pediatric patients, researchers elected to pursue PDL in darker skin types prior to CO_2 and LADD of TAC; however, they selected PDL fluence and CO_2 settings based on the individual's scar characteristics and, importantly, skin type.[81] Retrospective analysis revealed a significant difference between FSTs II and III and IV–VI PDL fluence (6.47 ± 0.25 J/cm2 and 6.25 ± 0.17 J/cm2, respectively).[81] Successful treatment with minimal adverse events in all groups, including darker skin types, was attributed to these individualized modifications.[81] Similar studies have been performed with keloid scars exclusively, demonstrating successful combination treatment of fractional CO_2 laser and topical TAC administration, with minimal recurrence, though notable side effects of telangiectasia and hyperpigmentation.[82]

Two case studies have also confirmed the efficacy of either laser-assisted corticosteroid delivery or LADD and intralesional corticosteroid administration, both of which supported the successful and safe treatment of keloids in patients with FST VI with improvement in cosmetic appearance and pain, with no adverse pigmentary changes.[83,84] The case study conducted by Kraeva et al suggests that topical corticosteroids following fractionally ablative laser might be responsible for the decreased risk of dyschromia that would otherwise be heightened following laser treatment in darker skin types.[83] Both of these studies, however, suggest the need for multiple sessions in order to produce significant and sustained results.[83,84] Other studies have gone a step further, demonstrating the safe LADD of both 5-FU and TAC, with no atrophy or pigmentary change in pediatric patients, one of whom had skin type IV.[85]

LADD application has been evaluated with medications beyond corticosteroids. Sabry et al explored the use of Botulinum toxin A, which paralyzes muscles in and near the scar site, both minimizing mechanical tension during collagen maturation and wound healing as well as modulating fibroblast activation patterns.[86,87] Sabry et al demonstrated that CO_2 laser-assisted botulinum toxin A delivery was efficacious for HTS, whereas intralesional injection was

successful for keloid scars in skin types III and IV.[86] Notably, the researchers hypothesized that statistically significant improvements in HTS from LADD may be confounded by the impact of the CO_2 laser itself, rather than botulinum toxin administration.[86] Further studies are necessary in order to determine whether laser therapy is mostly responsible for the clinical improvement seen in these studies or merely serves as an adjuvant for drug delivery.

Discussion

To date, the majority of scientific literature on treatment methods for HTS and keloids fails to specifically address patients with skin of color. Given the higher incidence of hypertrophic and keloid scarring in darker skin types, it is quite paradoxical that this particular population has been investigated only sparsely. Current literature seems to either 1) underrepresent patients of color in their study samples, 2) simply place a few such individuals of color within a larger sea of patients who are of lighter FSTs, or 3) fail to stratify results by skin type at all. As a result, external validity of treatment outcomes is often limited to patient populations of lighter skin types or not at all.

It is thus difficult to craft a universal clinical solution to HTS and keloids. In fact, regions consisting predominantly of people with higher FSTs have attempted to prescribe a standardized treatment algorithm for this group but have nonetheless been unable to account for all ethnic disparities.[88–90] This hesitancy to identify one such protocol to date should be used to support the claim that the nuances of these treatments should be heavily considered. This propensity to generalize is further complicated by differences in methodology, limitations in experimental design, provider disparities, etc. Nevertheless, current literature provides a foundation upon which to explore further.

The importance of individual patient characteristics (eg, scar characteristics, FST, past treatment efficacy, etc) in treatment selection is crucial. Results in studies yielding efficacious results have corroborated the criticality of modification of protocol on an individual basis. Beyond accounting for differences in patient characteristics, clinicians should be willing to also embrace a multimodal or multi-faceted approach to treatment. Combining treatments synergistically improves patient outcomes by simultaneously addressing multiple histopathological characteristics and patient-reported symptoms of scars, including dense and disorderly collagen, angiogenesis, pruritus, etc. Further research specifically within this population, however, is required in order to determine the best therapeutic option(s) and to work to define a more robust protocol based on these special considerations.

Conclusion

The quest to discover and refine therapies for the treatment of hypertrophic and keloid scarring in patients with skin of color is still ongoing. Upon a thorough analysis of the various methods—monotherapeutic and combinatorial—by which keloids and HTS can be treated, we would be remiss to advocate for just one. Due to a limited amount of literature and an inability to make completely objective comparisons across these studies, it must be suggested that providers evaluate the appropriate treatment modality (and its modulations) in order to make the best decision for the patient at hand. Nevertheless, it is clear that the various modalities by which each of these interventions act are unique. As such, it would seem logical to combine therapeutics, with attention paid to respective side effects, in order to target the distinctly different symptomatic facets of keloids and HTS. Further study in this niche field should remain a high priority in the realm of dermatology due to the lack of effective treatment options, currently sparse scientific investigation, and high prevalence of hypertrophic and keloid scarring in people of color specifically. Future studies on various multimodal approaches should be performed widely with clear clinical correlations made to FST, severity, recurrence, past treatment success, and individual patient characteristics in order to create a more robust clinical treatment guideline for HTS and keloid reduction in patients of color.

Abbreviations

FSTs, Fitzpatrick skin types; TGF-β, transforming growth factor beta; ECM, extracellular matrix; ET-1, endothelin-1; SCF, stem cell factor; triamcinolone acetonide; VSS, Vancouver Scar Scale; JSW, Japan Scar Workshop; POSAS, Patient and Observer Scar Assessment Scale.

Disclosure

The authors report no conflicts of interest in this work.

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